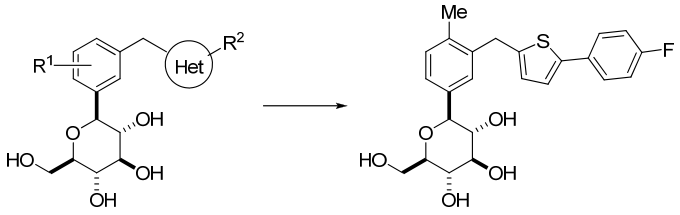
S38-1 Discovery of Canagliflozin as SGLT2 inhibitor for the Treatment of Type 2 Diabetes Mellitus

◯Sumihiro NOMURA[1], Shigeki SAKAMAKI[1], Mitsuya HONGU[1], Eiji KAWANISHI[1], Yuichi KOGA[1], Toshiaki SAKAMOTO[1], Yasuo YAMAMOTO[1], Kiichiro UETA[2], Hirotaka KIMATA[2], Keiko NAKAYAMA[2], Minoru TSUDA-TSUKIMOTO[3]

[1]Med. Chem., Mitsubishi Tanabe Pharma, [2]Pharmacology, Mitsubishi Tanabe Pharma, [3]DMPK, Mitsubishi Tanabe Pharma

The incidence of type 2 diabetes mellitus (T2DM) is markedly increasing in westernized societies and some developing countries. However, at present, no single agent is capable of achieving acceptable, long-lasting blood glucose control in the majority of patients. Accordingly, there is a strong incentive to develop novel drugs with improved efficacy and safety. Plasma glucose is filtered in the glomerulus and then reabsorbed in the proximal tubules in the kidney. Most of glucose reabsorption is mediated by sodium-dependent glucose cotransporter 2 (SGLT2). SGLT2 inhibitor, T-1095 orally enhances urinary glucose excretion and consequently lowers blood glucose levels independent of insulin action. We explored metabolically more stable *C*-glucosides bearing heteroaromatic ring than *O*-glucoside, T-1095, which resulted in the discovery of novel thiophene derivative TA-7284 (Canagliflozin). Synthesis, and biological profiles will be described.



Het: Heteroaromatic

TA-7284 (Canagliflozin)